19- (withdrawn) Method according to claim 1, wherein said topical ophthalmic solution is in the form of an aqueous solution and further contains one or more tonicity adjusting agents, one or more buffers and one or more antioxidants.

20- (withdrawn) Method according to claim 1, wherein said topical ophthalmic solution further contains one or more antimicrobial agents.

21- (withdrawn) The composition according to claim 1, wherein said dose is in pill form for oral administration.

22- (withdrawn) The method according to claim 1, wherein said topical ophthalmic solution further contains one or more combinations of NO donors and cGMP PDE5 inhibitors.

23- (withdrawn) The method according to claim 1, wherein said topical ophthalmic solution further contains one or more weight percentage combinations of NO donors and cGMP PDE5 inhibitors.

Thus the new set of claims are:

1- Method for lowering ocular hypertension, comprising administering, to a patient in need thereof, a topical ophthalmic eye drop or ointment containing NO releasing agent Pyrimidine and cGMP-PDE5 inhibitor Sildenafil Citrate.

2- Method according to claim 1, wherein said topical ophthalmic eye drop or ointment is in the form of an aqueous solution or suspension, or in the form a gel, or a cream in a pharmaceutically acceptable ophthalmic vehicle, or in the form of an erodible ocular insert or of a "reservoir" system with a polymer membrane or a gel to be placed in the conjunctival sac.

3-Methods according to claims 1 and 2, wherein the No releasing agent in said ophthalmic medicament is nitroglycerine.

4-Method according to claims 1and 2, wherein the No releasing agent in said ophthalmic medicament is sodium nitroprusside.

5-Method according to claims 1 and 2, wherein the cGMP specific PDE-5 inhibitor in said ophthalmic solution is (sildenafil) also known as 1-[[3-(6,7-dihydro-1 methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-- yl)-4 ethoxyphenyl]sulphonyl]-4-methylpiperazine.

These claims have been revised and amended or withdrawn based on examiners election/restrictions under 35 USC 121 or 35 USC 112.

Please consider the following remarks in support of the revised claims and in connection with rejections under 35 USC 103:

REMARKS

The essential reason for rejection of basic claims 1 and 2 by the examiner is that the

combination of NO donors and cGMP-PDE5 inhibitors to heal glaucoma is obvious to one skilled in the art, because Nathanson in 1992 (Journal of Pharmacology) teaches NO donors as hypotensive agents for glaucoma and in 2002, Laties teaches various cGMP-PDE5 inhibitors and in particular Sildenafil Citrate as treatment agent for glaucoma. Similarly, the examiner rejects claims 1 and 2 as obvious to one skilled in the art on the basis of Nathanson's paper in 1992 (Journal of Pharmacology) and a patent application of Scheman in which Scheman teaches how to treat retinal vein occlusion (RTV) by Sildenafil. We would like to address these issues and present reasons to the examiner that these rejections can be overcome. First in connection with Nathanson, we do agree that NO donors are hypotensive. However, our disclosure combines NO donors with cGMP-PDE5 inhibitors to enhance the effect of NO donors. Please refer to our sections 0009 and 0023 amongst others for detailed discussions on these issues. To simply argue it, cGMP-PDE5 does not by itself lower the ocular pressure and is not a hypotensive agent despite Laties claims, because it is not a vasodilator. All it does is that it inhibits the formation of enzyme PDE5 that specifically destroys enzyme cGMP, which is a vasodilator, produced by NO donors. These are fully explained in our disclosure and in particular sections 0009 and 0023. This synergistic combination was not obvious to Professor Nathanson in 1992 (Journal of Pharmacology), as the examiner has noted. However, Laties knew this combination but he chose not to claim it. Laties in I column 1, (section 005) and column 2, (section 0007) indicates that he is aware of the effect of NO donors in lowering IOP but maintains that he does not want to use NO donors in combination with cGMP-PDE5, because they make glaucoma worse (column 2, line 31-32 actually claims the combination works against glaucoma). Therefore, he intentionally avoids the combination of NO donors and cGMP-PDE-5 inhibitors and does not claim it. However, we must emphasize the fact that cGMP-PDE5 inhibitors do not act as vasodilators which is needed to treat glaucoma in order to dilate the Schlem's canal for enhanced aqueous humor drainage and lowering of IOP. All they do is to inhibit the formation of enzyme PDE5 that destroys cGMP enzyme (produced by NO donors) that causes vasodilation and treatment of glaucoma. The reason why cGMP-PDE5 in the form of Viagra works as erectile enhancer is not because it does vasodilation for erection and enhanced blood flow to the penis, but because it slows down the destruction of cGMP enzyme produced naturally by the body when arousal occurs by the enzyme PDE5 produced by the body to suppress it. In patients with glaucoma no such natural production of cGMP in the ophthalmic area (eye) is documented and thus using Viagra for glaucoma will not work by itself and there is no published document proving that. Laties is misled by the erectile dysfunction treatment effects of Viagra and assumes that the same will happen for glaucoma, namely vasodilation. We respectfully ask the examiner to consider our intricate medical points in this discussion and do not consider the NO donor+cGMP-PDE5 as an obvious issue.

On the 35 USC 103 rejection of our claims 1 and 2 on the basis of Nathanson's 1992 paper (Journal of Pharmacology) and patent application of Scheman (US 2003/0225101 A1) we must again respectfully argue that Scheman in his 19 claims never mentions or claims glaucoma treatment. True that he mentions (section 0012) RVO can lead to glaucoma and he claims treating RVO. However, even if he had directly claimed treatment of glaucoma, the above arguments in connection with Nathanson and Laties still applies to sildenafil, as well and will not be repeated again.

Having responded to each and every objection and rejection raised by the Examiner, it is believed that the patent application is now in condition for allowance, and such allowance is respectfully requested. If the Examiner has any questions or suggestions for expediting an allowance in this matter, the Examiner is invited to call the undersigned collect.

The Commissioner is authorized to charge any required fees, which may be required during the entire pendency of the application.

Respectfully submitted,

Dated: January 25, 2005

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